SUPPORT FOR THE AMENDMENTS

Applicants have replaced Claim 17 with new Claim 37. Support for new Claim 37 can be found in Claims 17 and 34, as previously presented and on page 7, lines 10-13, and from page 7, line 31, to page 8, line 32 of the specification. Applicants have also added new Claim 38. Support for new Claim 38 can be found on page 6, lines 21-28, of the specification. Support for the amendment to Claim 29 can be found on page 9, line 17, of the specification.

No new matter has been added. Claims 11, 14, 15, 18-33, and 35-8 are active in this application.

REMARKS/ARGUMENTS

The present claims relate to processes for the preparation of a dry powder formulation for the pulmonary administration of a micronized drug by means of a dry powder inhaler, said process comprising mixing coarse carrier particles having a starting diameter which lies between 20 and 1000 μm with fine carrier particles having a diameter of less than 10 μm, wherein said mixing step is carried out in a mixer with a stationary or rotating body equipped with a rotating element or in a high energy mixer.

The inventors have discovered that the presently claimed process provides a process for the preparation of a dry powder for the pulmonary administration of micronized drugs wherein the respirable fraction of the delivered dose of the drug is improved by maintaining good flowability characteristics of the powder, *i.e.*, characterized by a Carr's index of less than 25.

The technical problem is to reduce the interparticle forces between the micronized active drug and the carrier that can affect the availability of the drug to the respiratory tract, by maintaining suitable flowability properties.

The solution provided by the present claims is a process comprising adding the active ingredient to a carrier powder obtained by the presently claimed process which involves mixing coarse carrier particles having a starting diameter comprised between 20 and 1000 μm with fine particles with a diameter below 10 μm and, optionally, adding additive particles.

It has indeed been found that fine particles of a diameter below 10 μm, once redistributed onto the surface of the coarse carrier, decrease the interparticle forces without decreasing the flowability of the carrier powder and the presence of an additive further reduces the drug-carrier interparticle forces, thereby improving the respirable fraction. These effects are demonstrated in the present Examples.

The cited references contain no disclosure or suggestion of the presently claimed process. Accordingly, these references cannot affect the patentability of the present claims.

The rejection of Claims 11, 14, 15, and 17-36 under 35 U.S.C. § 103(a) in view of U.S. Patent No. 6,153,224 (Staniforth) in view of U.S. Patent No. 6,284,287 (Sarlikiotis et al) is respectfully traversed.

Staniforth discloses treating carrier particles by a milling process, preferably carried out in a ball mill (see, col. 9, lines 38-42). Milling, as reported on page 7, lines 19-25, of the present specification, is a hard process that dislodges asperities of the carrier particles in the form of small grains. Milling is an uncontrolled process that can be detrimental to the flowability properties of the powder.

In fact the Carr's index values of the samples of milled carrier particles of Staniforth, given in Table 4 on column 15, are much higher than 25, ranging from 32.1 to 36.4. Mixing is a milder process that applies a lower energy level to the surface of the carrier particles, whose flowability can be highly influenced by their surface characteristics.

Sarlikiotis et al does not teach or suggest to preparing a dry powder for pulmonary inhalation by mixing fine carrier particles having a diameter below 10 μm with coarse carrier

particles in order to decrease the interparticle forces between the active substance and the carrier particles and even less to add an additive in order to further improve the respirable fraction of the delivered drug, without affecting the flowability characteristics of the powder. Accordingly, there is nothing in Sarlikiotis et al which can cure the deficiencies of Staniforth.

Therefore it would not have been obvious at the time of the invention to provide the claimed mixing process to prepare dry powder compositions with good flowability properties and improved respirable fraction of the drug.

For all of these reasons, the rejection should be withdrawn.

The rejection of Claims 11, 14, 15, and 17-36 under the judicially-created doctrine of obviousness-type double patenting in view of Claims 1-21 of U.S. Patent No. 6,641,844 (Musa et al) has been obviated by appropriate amendment. As the Examiner will note, Applicants have amended the present claims such that they are not obvious in view of Musa et al or render the claims of Musa et al obvious. Accordingly, the rejection should be withdrawn.

Applicants submit that the present application is now in condition for allowance, and early notification of such action is earnestly solicited.

Respectfully submitted,

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